RULES AND REGULATIONS
GOVERNING NEWBORN SCREENING
AND BIRTH DEFECTS

Adopted by the Mississippi State Board of Health

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MISSISSIPPI STATE DEPARTMENT OF HEALTH
Genetic Screening Program
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SECTION I - AUTHORITY

A. **Statutory Authority**

Section 41-21-201 of the Mississippi Code of 1972, Annotated, authorizes the State Department of Health to adopt rules and regulations to carry out the Newborn Screening and Follow-up Program for hypothyroidism, phenylketonuria (PKU), hemoglobinopathy, congenital adrenal hyperplasia (CAH), galactosemia, and other such conditions as specified by the State Board of Health.

Section 41-24-1 of the Mississippi Code of 1972, Annotated, authorizes the State Department of Health to adopt rules and regulations to establish a program of testing to determine the presence of sickle cell trait or sickle cell anemia.

B. **Legal Requirements**

Under the statutory authority, the physician attending a newborn child, or the persons attending a newborn child who was not attended by a physician, is held responsible for ensuring that the child is tested for the newborn screening tests as described in these rules and regulations. State law exempts from these tests any child whose parents object thereto on the grounds that such tests conflict with their religious practices or tenets.

Under the statutory authority, screening for hypothyroidism (TSH), phenylketonuria (PKU), hemoglobinopathies (Hgb), congenital adrenal hyperplasia (CAH), and galactosemia (GAL) will be conducted statewide. Screening for the following conditions, as determined and specified by the State Board of Health, will also be conducted:

Biotinidase Deficiency
Cystic Fibrosis

Argininemia
Argininosuccinic Aciduria (ASA Lyase Deficiency)
Carbamoylphosphate Synthetase Deficiency (CPS Deficiency)
Carnitine Palmitoyltransferase I Deficiency (CPT I)
Carnitine Palmitoyltransferase II Deficiency (CPT II)
Carnitine/Acylcarnitine Translocase Deficiency (Translocase)
Citrullinemia (ASA Synthetase Deficiency)
Glutaric Aciduria Type I (GA I)
Homocystinuria
3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG)
Hyperammoninemia, Hyperornithinemia, Homocitrullinemia Syndrome (HHH)
Hypermethioninemia

_____Isobutyryl-CoA Dehydrogenase Deficiency
Isovaleric Acidemia (IVA)
Long-Chain 3-hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)
Malonic Aciduria
Maple Syrup Urine Disease (MSUD)
Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCAD)
2-Methylbutyryl-CoA Dehydrogenase Deficiency
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC Def)
3-Methylglutaconyl-CoA Hydratase Deficiency
Methylmalonic Acidemia (MMA)
Mitochondrial Acetoacetyl-CoA Thiolase Deficiency
Multiple Acyl-CoA Dehydrogenase Deficiency (MADD or GA II)
Multiple CoA Carboxylase Deficiency
5-Oxoprolinuria (Pyroglutamic aciduria)
Propionic Acidemia (PPA)
Short-Chain Acyl-CoA Dehydrogenase Deficiency (SCAD)
Short-Chain Hydroxy Acyl-CoA Dehydrogenase Deficiency (SCHAD)
Trifunctional Protein Deficiency (TFP Deficiency)
Tyrosinemia Type I (TYR I)
Tyrosinemia Type II (TYR II)
Very Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)

SECTION II - SPECIMEN COLLECTION

A. **Specimen Requirements**

1. The specimen must be dried blood spots for screening and whole blood for confirmatory testing.

2. Newborn Screening must be performed prior to hospital discharge. Any specimen collected prior to 24 hours of age will require repeat specimen collection.

3. Newborn Screening collection for GAL and Hgb are accepted for testing under the assumption that the infant has had a lactose feeding and has not been transfused. This statement is noted on Mississippi's lab slip, Form No. PH 1582.

4. The performing lab must receive the specimen within five working days. All specimens requiring repeat testing will be monitored by the genetics program as follows:
    a. Specimens repeated due to lack of information will be the responsibility of the originating hospital.
    b. All other repeat specimens will be followed by the patient's local county health department.

5. Mississippi State Department of Health Form PH-1582 or an identical form must be completed in full and accompany the specimen. It is critical that the data on the form be accurate; the information entered must be compatible with that recorded on the infant's birth certificate. The form must be completed according to the instructions issued by the Mississippi State Department of Health Genetic Screening Program.

B. **Fees**

A charge of $70.00 will be assessed for every infant screened to defray the cost of maintaining a central registry, for lab testing and for health department follow-up on positive and repeat tests.

SECTION III - FOLLOW-UP

A. The Genetic Screening Program will be responsible for assuring that all infants with positive, questionable, and repeat screening tests are appropriately followed. Follow-up on infants who have a private physician will be coordinated with the physician; the local health department will provide repeat follow-up on all specimens that have been collected too early or improperly.

B. If the newborn screening tests have to be repeated due to lack of information on the lab slip, the hospital will be charged with finding the newborn and repeating the newborn screening tests.

SECTION IV - LABORATORY REQUIREMENTS

A. **Compliance with Standards**

All laboratories which plan to offer this testing must meet those standards outlined in this section and provide the agency with a written statement that they will comply with these standards. All specimens must be tested in an approved laboratory located in the United States .

Because the results of hemoglobinopathy, galactosemia, and congenital adrenal hyperplasia screening are not always clear cut and because this type of screening requires extensive input from a recognized reference laboratory, a single control screening laboratory is required. The National Institutes of Health quotes:

> "The panel recommends centralized laboratories for mass screening programs and for confirmation of diagnosis because of large numbers of samples."

B. **Specimen Requirements**

Specimens acceptable for analysis include only dried blood spots for newborn screening, and whole blood or serum for confirmatory testing.

C. **Method for Specimen Analysis**

1. PKU
   By a continuous flow chemistry analysis or by tandem mass spectrometry analysis

2. Hypothyroidism
   TSH - EIA method

3. Hemoglobinopathy
   By iso-electric focusing electrophoresis

4. Galactosemia
   (a) By a continuous flow chemistry analysis
   (b) Gal 1, G-PUT Deficiency Screening Test

5. CAH
   17-alpha-hydroxy-progesterone (17-OHP) levels - EIA method

6. Other Disorders
   By tandem mass spectrometry analysis, or by biochemical and other conventional methods

D. **Quality Control**

1. The laboratory must be successfully participating in an acceptable proficiency testing program that will monitor the performance of all testing methodologies. Acceptable testing programs are the following:
   (a) College of American Pathologists (CAP)
   (b) American Association of Clinical Chemists (AACC)
   (c) Centers for Disease Control (CDC)

2. Reagents used by the laboratory must be FDA approved.

3. The laboratorian must examine the quality and integrity of blood spots and must have a written procedure for rejection of those specimens judged to be unacceptable.

4. The laboratory must be testing a minimum of 50,000 specimens per year for each disorder.

5. Standard curves must be done with each assay of TSH and CAH.

6. For TSH and CAH testing, normal, borderline, and high controls must be included in each run.

7. All infants not considered normal (low birth weight, premature, etc.) should be excluded from statistical calculations for the geometric mean and cutoff values for TSH. These omitted values should be compared with a composite accumulated data set from the same population.

8. Since interpretation of 17-OHP levels for CAH is weight dependent, a current weight in grams must be documented for all specimens submitted for CAH testing.

9. Laboratories must be Medicare approved.
   (Laboratories must have either a certificate or a certificate of registration from the Health Care Financing Administration (HCFA) as mandated by the Clinical Laboratory Improvement Amendments (CLIA) of 1988.)

10. Hemoglobinopathies
    (a) Control(s) containing AFSC and FAS must be included in each assay.
    (b) All samples that are not normal (not Hb AA) must be sent to a recognized reference laboratory as liquid blood.

(c) A random sample will be sent each month to the reference facility for confirmation.
(d) If transfused, retested on a liquid blood sample at 3 months post last transfusion.

E. **Disorders being Screened**

PHENYLKETONURIA
Phenylketonuria is a genetic disorder inherited as an autosomal-recessive trait caused by the absence of an enzyme that is necessary for metabolism of the essential amino acid phenylalanine. If untreated, neurologic deterioration, seizures, and severe mental retardation will occur. It affects one in every 10,000 live births.

HYPOTHYROIDISM
Hypothyroidism is a disorder in which there is a decrease in the production of thyroid hormone, possibly resulting in brain damage and mental retardation in the absence of prompt treatment. The national average is approximately one congenital hypothyroid newborn for every 4,000 births.

HEMOGLOBINOPATHIES
Hemoglobinopathy, which includes sickle cell diseases, thalassemia, and other variants are blood disorders resulting from change in the structure of hemoglobin. Sickle Cell Disease, the most common hemoglobinopathy in Mississippi, is an inherited disease found primarily in African-Americans and people of Mediterranean descent. Although there is no cure for sickle cell disease, early detection is important for effective treatment and prevention of complications. Infection due to Streptococcus pneumonia is a significant cause of death during the first few years of life for patients with sickle cell disease. One in every ten African-Americans has some form of trait and one out of 400 have sickle cell disease.

GALACTOSEMIA
Galactosemia is an inborn error of metabolism, inherited as an autosomal-recessive trait, in which the hepatic enzyme galactose-1-phosphate uridyl transferase is absent, preventing the conversion of the milk sugar galactose to glucose. If untreated death can occur in the first month of life. Galactosemia occurs in one of 50,000 live births in the United States.

CONGENITAL ADRENAL HYPERPLASIA

Congenital Adrenal Hyperplasia is a genetic endocrine disorder caused primarily by a deficiency of enzymes needed for the adrenal glands to make the hormones cortisol and aldosterone. It can result in masculinization of female genitalia as well as adrenal crisis and early infant death. CAH occurs in one out of every 16,000 births.

BIOTINIDASE DEFICIENCY

CYSTIC FIBROSIS

DISORDERS DETECTABLE VIA TANDEM MASS SPECTROMETRY

A tandem mass spectrometer is an analytical instrument consisting of two mass spectrometers in series connected by a reaction chamber or collision cell. It can identify a compound by its mass and determine how much of the compound is present. Through tandem mass spectrometry analysis, many genetic disorders can be detected from one blood specimen.

F. **Record Retention**

Records of standardization, quality control, and patient values must be kept for at least two years. It is advisable for laboratories to retain these records until the statute of limitations regarding medical malpractice actions expires as stipulated by Mississippi state law.

SECTION V - BIRTH DEFECTS REGISTRY

A. Authority

1. **Statutory Authority**
Section 41-21-205 of the Mississippi Code of 1972, Annotated, authorizes the State Department of Health (the department) to adopt rules and regulations to govern the operation of the Birth Defects Registry.

2. **Legal Requirements**
Under the statutory authority, the Board of Health (the board) shall:

- establish in the department a program to;
  (a) identify and investigate birth defects, and
  (b) maintain a central registry of cases of birth defects

- design the registry program that will;
  (a) provide information to identify risk factors and causes of birth defects,
  (b) provide information on other possible causes of birth defects,
  (c) provide for the development of strategies to prevent birth defects,
  (d) provide for interview studies about the causes of birth defects, and
  (e) provide for the collection of birth defect information

- adopt rules, regulations and procedures to govern the operation of the registry program and to carry out the intent of this action

- specify the types of information to be provided to the birth defects registry and the persons and entities who are required to provide such information to the birth defects registry

- prescribe the manner in which records and other information are made available to the department

- obtain records and/or test results of individuals not reported or observed to have a birth defect reported to the department at a later date

- collect, analyze and place data in a central registry to facilitate research and to maintain security

- use the registry to;
  (a) investigate the causes of birth defects and other health conditions as authorized by statute,
  (b) design and evaluate measures to prevent the occurrence of birth defects, and other conditions, and
  (c) conduct other investigations and activities necessary for the board and the department to fulfill their obligation to protect the public health

3. **The Birth Defects Advisory Committee**
The State Health Officer may appoint or delegate his authority for the purposes of this section to an advisory committee, not to exceed (10) persons, to assist in the design and implementation of this central registry with representation from relevant groups including, but not limited to, hospitals, physicians, board-certified clinical geneticists, personnel of the department, personnel of other appropriate state agencies, disabled persons and parents of disabled children (resulting from a birth defect). If a central registry advisory committee is created by the State Health Officer, the board shall consult and be advised by the committee on the promulgation of rules, regulations and procedures for the purposes of this section.

B. Identifying Reportable Cases

1. **Definition of Birth Defect**
A birth defect is an abnormality of structure, function or metabolism, whether genetically determined or a result of environmental influences during embryonic or fetal life. A birth defect may present from the time of conception through one year after birth, or later in life.

a. From birth to one year of age certain principal birth defects shall be reported.

b. Other defects found later in life may be reported at any time.

2. **Reportable Birth Defects**
Live Births and Reportable Fetal Deaths with birth defects (fetal death of

20 completed weeks of gestation or more, or a weight of 350 grams or more) shall be reported. Birth Defects of the following categories must be reported:

Craniofacial	GI/GU
Neural Tube	Teratogen
Cardiac	Skeletal
Genetic Disorders	Skin
Congenital Tumors	Central Nervous System

3. **Persons and entities required to provide information to the Registry**

a. The physician must report every birth defect case the first time the patient is seen, beginning January 1, 2000. A reporting card (See Attachment A) or its equivalent as determined by the Mississippi State Department of Health is required whether or not the birth defect was diagnosed. If the patient is seen for another birth defect on another occasion, that defect would also need to be reported.

b. Appropriate birth certificate data will be reported.

c. Appropriate data from other department registries such as the Cancer Registry and Newborn Hearing Registry will be reported.

d. Newborn discharge summaries from the state's tertiary care center will report data.

4. **Criteria for Inclusion as a Case**

a. The infant/fetus must have a reportable structural defect, newborn screening disorder, functional or metabolic disorder, genetically determined or a defect resulting from an environmental influence during embryonic or fetal life.

b. The defect should be diagnosed or its signs and symptoms recognized within the first year of life. This age range may be extended, as approved by the advisory committee.

c. An infant must have been born alive or a fetus must have gestational age of at least 20 weeks or a birth weight of at least 350 grams to be included.

5. **Process for making records and other information available to the Registry**

a. The department may obtain records and/or test results of individuals not reported or observed to have a birth defect reported to the department at a later date.

b. The following persons who act in compliance with this section are not civilly or criminally liable for furnishing the information required under this section:

- A hospital, clinical laboratory, genetic treatment center or other health care facility;
- An administrator, officer or employee of a hospital, clinical laboratory, genetic treatment center or other health care facility; and
- A physician or employee of a physician.

c. The department field staff will visit health care facilities to gather medical information of children with birth defects. They will record this information on registry data report forms (See Attachment B) on potentially reportable conditions to be added to the registry.

6. **Confidentiality and Security**

a. Information collected and analyzed by the department under this section shall be placed in a central registry to facilitate research and to maintain security.

- Data obtained under this section directly from the medical records of a patient is for the confidential use of the department and the persons or public or private entities that the department determines are necessary to carry out the intent of this section. The data is privileged and may not be divulged or made public in a manner that discloses the identity of an individual whose medical records have been used for obtaining data under this section.

- Information that may identify an individual whose medical records have been used for obtaining data under this section is not available for public inspection under the Mississippi Public Records Act of 1993.

- Statistical information collected under this section is public information.

b. Misuse of the Registry Data:

- Any person or entity who misuses the information provided to the registry shall be subject to a civil penalty of Five Hundred Dollars ($500.00) for each such failure or misuse. Such penalty shall be assessed and levied by the board after a hearing, and all such penalties collected shall be deposited into the State General Fund.

7. **Policies and Procedures**
The department will publish written policies and procedures to guide the operations of the registry.

ATTACHMENT A

MANDATED BIRTH DEFECTS REPORTING CARD

ATTACHMENT B

MISSISSIPPI BIRTH DEFECTS REGISTRY DATA REPORT